Darapladib Ineffective at Reducing Major Coronary Events After ACS

Written by Nicola Parry

Michelle O'Donoghue, MD, Brigham and Women's Hospital, Boston, Massachusetts, USA, presented primary results from The Stabilization of Plaques Using Darapladib-TIMI 52 trial [SOLID-TIMI 52; NCT01000727], demonstrating that darapladib is ineffective at reducing major coronary events when started within 30 days after an acute coronary syndrome (ACS) event.

By way of background, lipoprotein-associated phospholipase A_2 (Lp-PLA_2), a calcium-independent phospholipase A_2 that circulates in plasma in association with low-density lipoprotein particles, has been hypothesized to play a causal role in the development of atherosclerosis and to contribute to plaque instability through pathways related to inflammation. Darapladib is an enteric-coated, direct Lp-PLA_2 inhibitor that reduces enzyme activity in plasma and atherosclerotic plaques [Boekholdt SM et al. *Circulation.* 2008].

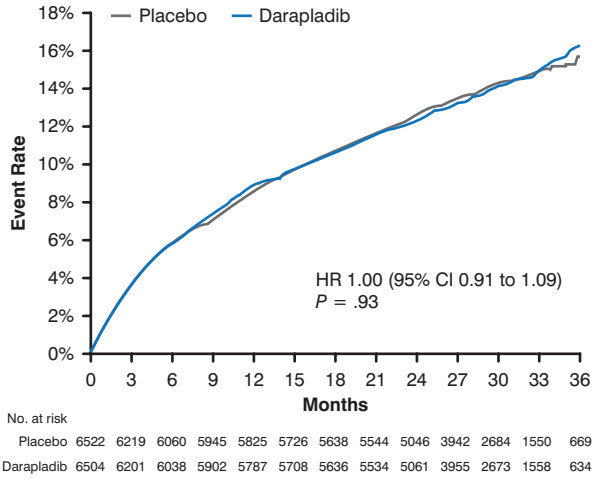
The SOLID-TIMI 52 trial was a double-blind, placebo-controlled, phase 3 study that was conducted at 868 sites in 36 countries to compare the safety and efficacy of darapladib with placebo for patients with ACSs if started within 30 days after hospitalization. It enrolled 13 026 participants within 30 days of hospitalization with ACSs. Qualifying events were most commonly STEMI (45.2%), NSTEMI (42.7%), and unstable angina (12.2%) and were balanced between the darapladib and placebo treatment arms.

Participants were randomized 1:1 to darapladib (160 mg once daily; n = 6504) or matching placebo (n = 6522), with a median follow-up duration of 2.5 years. The primary end point was the composite of coronary heart disease (CHD) death, myocardial infarction (MI), or urgent coronary revascularization for myocardial ischemia. Secondary end points included the composite of cardiovascular (CV) death, MI, or stroke; total coronary events; CHD death or MI; any coronary revascularization; individual components of the primary end point; and all-cause mortality.

After 3 years, the results demonstrated no significant difference in the occurrence of the primary end point between participants in the darapladib and placebo arms (16.3% vs 15.6%; HR, 1.00; 95% CI, 0.91 to 1.09; *P* = .93; Figure 1).

Similarly, darapladib did not significantly reduce the risk for the study's secondary end points of CV death, MI, or stroke (15.0% vs 15.0%; HR, 0.99; 95% CI, 0.90 to 1.09; *P* = .78). Additionally, there were no significant differences between the treatment arms for the individual components of the primary end points, for additional secondary and exploratory end points, or all-cause mortality (7.3% vs 7.1%; HR, 0.94; 95% CI, 0.82 to 1.08; *P* = .40).

Figure 1. Occurrence of the Primary End Point in the Darapladib and Placebo Treatment Arms



CHD, coronary heart disease; MI, myocardial infarction.
Reproduced with permission from M. O'Donoghue, MD.

Participants in the darapladib arm reported an odor-related complaint (predominantly of the urine, feces, and skin; 11.5% vs 2.5%) and diarrhea (10.6% vs 5.6%) more frequently than those in the placebo arm.

These data therefore do not support a strategy of targeted Lp-PLA_2 inhibition with darapladib on a background of optimal medical therapy in patients stabilized after ACS events, concluded Dr O'Donoghue. However, ongoing trials are evaluating the clinical utility of other novel therapeutics that target alternative pathways of inflammation.

Prehospital Ticagrelor Reduces Stent Thrombosis in STEMI

Written by Emma Hitt Nichols, PhD

Administration of ticagrelor in-ambulance resulted in reduced rates of stent thrombosis in patients with STEMI undergoing percutaneous coronary intervention (PCI) compared with patients who received ticagrelor in-hospital; however, the co–primary end points were not achieved. Gilles Montalescot, MD, PhD, Centre Hospitalier Universitaire Pitié-Salpêtrière, Paris, France, presented data from the 30-Day Study to Evaluate Efficacy and Safety of Pre-hospital vs In-hospital Initiation of Ticagrelor Therapy in STEMI Patients Planned for PCI [ATLANTIC; NCT01347580].